RECEIVED CENTER

OCT 1 6 2008

Applicants: Christophorus Meijer et al.

Serial No : 10/551,584 Filed: September 29, 2005

Page 2

Amendments to the Claims

The following lists all pending claims as amended.

- 1. (Withdrawn) A method of detecting an HPV-induced invasive cancer or precursor lesion thereof associated with tumor suppressor lung cancer 1 (TSLC1) in a subject in need thereof, the method comprising contacting a cell component of a test cell of the subject with a reagent that detects the level of the cell component in the test cell and determining a modification in the level of the cell component in the test cell as compared with a comparable healthy cell, wherein the cell component indicates the level of TSLC1 in the cell and wherein a decrease in the level of TSLC1 indicates the presence of an HPV-induced invasive cancer or precursor lesion thereof.
- (Withdrawn) A method according to claim 1, wherein the HPV-induced invasive cancer or precursor lesion thereof is invasive cervical cancer or a premalignant cervical lesion with invasive potential.
- (Withdrawn) A method according to claim 1 or 2, wherein the HPV-induced invasive cancer is a high-risk HPV-induced invasive cancer.
- 4. (Withdrawn) A method according to claim 3, wherein the cell component is a nucleic acid associated with production of TSLC1 polypeptide, and the reagent targets the nucleic acid in the test cell, and the nucleic acid encodes the TSLC1 and regulatory regions.

Serial No : 10/551,584 Filed: September 29, 2005

Page 3

(Withdrawn) A method according to claim 4, wherein the nucleic acid is RNA. 5.

(Withdrawn) A method according to claim 4, wherein the reagent is a 6.

restriction endonuclease.

(Withdrawn) A method according to claim 5, wherein the reagent is a nucleic 7.

acid probe or primer that binds to the nucleic acid, having a detectable label.

(Withdrawn) A method according to claim 7, wherein the nucleic acid probe 8.

has a one of the following nucleotide sequences:

a polynucleotide sequence capable of hybridizing under stringent a)

conditions to the 5' regulatory region or the coding region of the TSCL1

sequence as set forth in Figure 1;

a polynucleotide sequence having at least 70% identity to the b)

polynucleotide of a);

a polynucleotide sequence complementary to the polynucleotide

sequence of a); [and] or

a polynucleotide sequence comprising at least 15 bases of a d)

polynucleotide sequence of a) or b).

(Withdrawn) A method according to claim 8, wherein the cell component is a 9.

polypeptide and the reagent targets the polypeptide in the test cell, and

Oct-16-08 03:55pm From-

Applicants: Christophorus Meijer et al.

Serial No.: 10/551,584 Filed: September 29, 2005

Page 4

wherein the polypeptide is TSLC1 and the reagent is an anti-TSLC1 antibody.

- (Withdrawn) A method according to claim 2, wherein the method of detecting evaluates the methylation status of the TSLC1 promoter.
- or a precursor lesion thereof associated with tumor suppressor lung cancer 1 (TSLC1) in a subject, the method comprising contacting a target cellular nucleic acid component of in a test cell with a reagent that detects TSLC1, and detecting a reduction in the TSLC1 in the test cell as compared to that of a comparable normal cell, detection an increased detecting an increase or decrease in methylation of the TSCL1 promoter in the test cell, a reduced production of TSLC1—in the test cell as compared to the a comparable normal cell is determined, or both.
 - (Previously Presented) A method according to claim 11, wherein the target cellular component is a nucleic acid.
 - 13. (Previously Presented) A method according to claim 12, wherein the nucleic acid is mRNA.
 - 14. (Withdrawn) A method according to claim 11, wherein the target cellular

Serial No : 10/551,584 Filed: September 29, 2005

Page 5

component is a protein.

- 15. (Previously Presented) A method according to claim 11, wherein the reagent is a nucleic acid probe or primer that binds to TSLC1.
- (Withdrawn) A method according to claim 14, wherein the reagent is an anti-TSLC1 antibody.
- 17. (Currently Amended) A method according to claim 14, wherein the subject has loss of heterozygosity at chromosome 11q23.
- 18. (Withdrawn) A method of treating HPV-induced invasive cancers and their precursor lesions associated with modification of TSLC1 production in cells in a subject afflicted with such a cancer or lesion, the method comprising contacting cells of the subject with a therapeutically effective amount of a reagent that increases TSLC1 level in the cells of the subject.
- 19. (Withdrawn) A method according to claim 18, wherein the reagent includes is a polynucleotide sequence comprising a TSLC1 sense polynucleotide sequence, preferably said polynucleotide is the native,—unmethylated TSLC1 sense sequence.
- 20 (Withdrawn) A method according to claim 19, wherein a nonmethylatable analog is substituted for cytidine within the TSLC1 sense sequence, said

Serial No : 10/551,584

Filed: September 29, 2005

Page 6

and wherein the nonmethylatable analog preferably being is 5-azacytadine.

- 21. (Withdrawn) A method according to claim 20, wherein the polynucleotide sequence is contained in an expression vector, and the expression vector is a plasmid, a viral particle or a phage.
- 22. (Withdrawn) A molecular diagnostic marker for detection of progression to invasiveness of HPV-induced premalignant lesions associated with tumor suppressor lung cancer 1 (TSLC1) and for detection of future metastatic potential of HPV-induced premalignant lesions and carcinomas associated with tumor suppressor lung cancer 1 (TSLC1), wherein the marker indicates TSLC1 promoter methylation, expression of mRNA associated with production of TSLC1 polypeptide, or both.
- 23. (Withdrawn) A kit for use in a method of detecting HPV-induced invasive cancers and their precursor associated with tumor suppressor lung cancer 1 (TSLC1) in test cells of a subject, the kit comprising means to collect test cells and the molecular diagnostic marker of claim 22.
- 24. (Withdrawn) A kit for use in a method of detecting HPV-induced invasive cancers and their precursor lesions associated with tumor suppressor lung cancer 1 (TSLC1) in test cells of a subject, the kit comprising primers and probes capable of hybridizing to TSLC1 nucleotide sequence of Figure 1,

Serial No: 10/551,584 Filed: September 29, 2005

Page 7

TSLC1 antibodies, or methylation sensitive restriction enzymes recognizing the sequence as described in Figure 1.

- (Withdrawn) A kit according to claim 23, wherein the test cells are cervical 25. cells.
- (Withdrawn) A method according to claim 5, wherein the RNA is mRNA. 26.
- (Withdrawn) A method according to claim 6, wherein the reagent is a methylation 27. sensitive restriction endonuclease.
- (Withdrawn) A method according to claim 19, wherein the polynucleotide is the 28. native, unmethylated TSLC1 sense sequence.